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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/967,305	09/28/2001	Jennifer Richardson	07334-312001 / MPI2000-31	5199

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/967,305	RICHARDSON ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,34 and 59-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-34, 59-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The finality of the previous Office action has been withdrawn, and the prosecution of this application is reopened to include new rejections raised upon further consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 33-34, 59-79 are being examined.

New Rejections Based on New Consideration

Objection

Claims 66-72 are objected to, for the use of the language " comprises at least 260, 300, 400, 500, 800, 900, or 1000 nucleotides of the full length complement of SEQ ID NO:3". It is not clear whether the nucleotide probe for use in the claimed method is composed of consecutive nucleotides or of non-consecutive nucleotides. This objection could be obviated by amending the claims, for example, to recite "consecutive nucleotides".

Claim Rejections - 35 USC § 112, Second Paragraph, New Rejection

Claims 33-34, 59-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33-34, 59-79 are indefinite for the use of the language "corresponding" in claim 33. In view that there is no definition of "corresponding", it is not clear what type of correspondence is referred to.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description,

New Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-34, 59-79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 33 is drawn to: A method for identifying candidate therapeutic agents for treating prostate cancer, comprising obtaining a test sample comprising metastatic prostate tumor cells and measuring the level of expression of alpha-methylacyl-CoA racemase mRNA "corresponding" to the nucleotide sequence of SEQ ID NO:3, wherein the test compound is identified as a candidate therapeutic agent if the level of expression of the alpha-methylacyl-CoA racemase mRNA in the test sample is less than that of a control test sample.

Claim 34 is drawn to: The method of claim 33, wherein the test sample is exposed to a nucleic acid probe which hybridizes to SEQ ID NO:3 under hybridization in 05.M sodium phosphate, 7% SDS at 65^0 C, and one or more washes at 0.2 X SSC, 1% SDS at 65^0 C, wherein the probe "comprises" a fragment of the full-length complement of SEQ ID NO:3.

Claim 59 is drawn to: The method of claim 33, comprising contacting alpha-methylacyl-CoA racemase mRNA with a nucleic acid probe "comprising" a fragment of the full-length

complement of SEQ ID NO:3, wherein said fragment "comprises" at least 15 consecutive nucleotides of the full-length complement of SEQ ID NO:3.

Claims 60-72 are drawn to the method of claim 59, wherein the probe comprises at least 20, 25, 30, 40, 50, 75 consecutive nucleotides or at least 260, 300, 400, 500, 800, 900, or 1000 nucleotides of the full length complement of SEQ ID NO:3.

Claims 73, 76, 77 are drawn to the method of claim 59, wherein the probe is immobilized on a surface (claim 73), wherein the probe is detectably labeled (claim 76), and wherein the detectable label is a chemiluminescent, a fluorescent, a radioactive, or a colorimetric label (claim77).

Claims 74, 78-79 are drawn to the method of claim 34, wherein the alpha-methylacyl-CoA racemase mRNA is immobilized on a surface (claim 74), wherein the probe is detectably labeled (claim 78), and wherein the detectable label is a chemiluminescent, a fluorescent, a radioactive, or a colorimetric label (claim79).

Claim 75 is drawn to the method of claim 33, comprising amplification of the alpha-methylacyl-CoA racemase mRNA.

The specification discloses sequences of two human alpha-methylacyl-CoA racemase sequences with an alternative amino acid at position 9, and of 3 known spliced variants thereof (SEQ ID NO:3, 4, 6, 8, 10, p.1, last paragraph, bridging p.2). The specification discloses that SEQ ID NO:3 of 1146 nucleotide in length is the open reading frame (i.e. a series of triplets coding for amino acids without any termination codons) of the human alpha-methylacyl-CoA racemase cDNA SEQ ID NO:1 of 2005 nucleotides in length (p.11, figure 1 legend). It is noted that it is not clear whether SEQ ID NO:3 is a complete sequence, because it is not clear that the

amino acid sequence encoded by SEQ ID NO:3 is a complete protein, having the function of the alpha-methylacyl-CoA racemase, in view that SEQ ID NO:3 is only an ORF with 1146 nucleotides in length of the cDNA SEQ ID NO:1, with 2005 nucleotides in length, without any termination coding.

Although the specification discloses sequences of some alpha-methylacyl-CoA racemase mRNA variants, however, since "corresponding" is not defined in the specification, alpha-methylacyl-CoA racemase mRNA "corresponding" to the nucleotide sequence of SEQ ID NO:3 encompasses any variants of the methylacyl-CoA racemase mRNA, with unknown structure and function, in view a lack of a disclosure of which region of SEQ ID NO:3 confers the methylacyl-CoA racemase function of SEQ ID NO:3. Further, since there is no common structure disclosed for the methylacyl-CoA racemase mRNA variants, the disclosed variants in the specification are not reprentative species. Further, due to the open language "comprises", the probes for use in the claimed method encompasses unknown sequences attached to a fragment complementary to SEQ ID NO:3.

In this case, the specification does not describe the variant alpha-methylacyl-CoA racemase mRNAs, or the probes that hybridize to SEQ ID NO:3, in a manner that satisfies either the standards as shown in the example of Lilly or Enzo. The specification does not provide sufficient structure or common structure, other than SEQ ID NO:3, 4, 6, 8, 10, to support the broad breath of the claimed genus. Nor is there any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses SEQ ID NOs: 3, 4, 6, 8, 10, this does not provide a description of the the variant alpha-

methylacyl-CoA racemase mRNAs, or the probes that hybridize to SEQ ID NO:3 that would satisfy the standard as shown in the example of Enzo.

The specification also fails to describe the variant alpha-methylacyl-CoA racemase mRNAs, or the probes that hybridize to SEQ ID NO:3, by the standards shown in the example in Lilly. The specification describes only SEQ ID NOs:3, 4, 6, 8, 10, without disclosure of common structure. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The specification does not provide an adequate written description of the variant alpha-methylacyl-CoA racemase mRNAs, or the probes that hybridize to SEQ ID NO:3, that is required to practice the claimed invention. Thus, the specification does not meet the 112, first paragraph written description requirement, and one of skill in the art would reasonably conclude that Applicant did not have possession of the claimed genus of variant alpha-methylacyl-CoA racemase mRNAs, or the claimed genus of probes that hybridize to SEQ ID NO:3, at the time the invention was made. Since the specification fails to adequately describe the product for use in the claimed method, it also fails to adequately describe the claimed method.

Claim Rejections - 35 USC § 112, Scope of Enablement, New Rejection

Claims 33-34, 59-79 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying candidates therapeutic agents, comprising measuring the mRNA level of the alpha-methylacyl-CoA racemase SEQ ID NO:3, does not reasonably provide enablement for a method for identifying candidates therapeutic agents, comprising measuring the expression level of the alpha-methylacyl-CoA racemase

"corresponding" to SEQ ID NO:3, using a probe that hybridizes to SEQ ID NO:3 under the conditions cited in claim 34, wherein the probe "comprises" a fragment of the full length complement of SEQ ID NO:3, or "comprises" at least 20, 25, 30, 40, 50, 75 consecutive nucleotides or at least 260, 300, 400, 500, 800, 900, or 1000 nucleotides of the full length complement of SEQ ID NO:3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claim 33 is drawn to: A method for identifying candidate therapeutic agents for treating prostate cancer, comprising obtaining a test sample comprising metastatic prostate tumor cells and measuring the level of expression of alpha-methylacyl-CoA racemase mRNA "corresponding" to the nucleotide sequence of SEQ ID NO:3, wherein the test compound is identified as a candidate therapeutic agent if the level of expression of the alpha-methylacyl-CoA racemase mRNA in the test sample is less than that of a control test sample.

Claim 34 is drawn to: The method of claim 33, wherein the test sample is exposed to a nucleic acid probe which hybridizes to SEQ ID NO:3 under hybridization in 05.M sodium phosphate, 7% SDS at 65^0 C, and one or more washes at 0.2 X SSC, 1% SDS at 65^0 C, wherein the probe "comprises" a fragment of the full-length complement of SEQ ID NO:3.

Claim 59 is drawn to: The method of claim 33, comprising contacting alpha-methylacyl-CoA racemase mRNA with a nucleic acid probe "comprising" a fragment of the full-length complement of SEQ ID NO:3, wherein said fragment "comprises" at least 15 consecutive nucleotides of the full-length complement of SEQ ID NO:3.

Claims 60-72 are drawn to the method of claim 59, wherein the probe comprises at least 20, 25, 30, 40, 50, 75 consecutive nucleotides or at least 260, 300, 400, 500, 800, 900, or 1000 nucleotides of the full length complement of SEQ ID NO:3.

Claims 73, 76, 77 are drawn to the method of claim 59, wherein the probe is immobilized on a surface (claim 73), wherein the probe is detectably labeled (claim 76), and wherein the detectable label is a chemiluminescent, a fluorescent, a radioactive, or a colorimetric label (claim77).

Claims 74, 78-79 are drawn to the method of claim 34, wherein the alpha-methylacyl-CoA racemase mRNA is immobilized on a surface (claim 74), wherein the probe is detectably labeled (claim 78), and wherein the detectable label is a chemiluminescent, a fluorescent, a radioactive, or a colorimetric label (claim79).

Claim 75 is drawn to the method of claim 33, comprising amplification of the alpha-methylacyl-CoA racemase mRNA.

The following *Wands* factors have been considered when the 112, first paragraph, scope of enablement rejection was made.

The breadth of the claims

The breadth of the claims is broad.

Since "corresponding" is not defined in the specification, alpha-methylacyl-CoA racemase mRNA "corresponding" to the nucleotide sequence of SEQ ID NO:3 encompasses any variants of the methylacyl-CoA racemase mRNA, with unknown structure, and function, supra, having unknown expression level in prostate cancer. Further, due to the open language "comprises", the probes for use in the claimed method encompasses unknown sequences

attached to a fragment complementary to SEQ ID NO:3, supra. In addition, since a tumor encompasses any enlargement or abnormal growth, which is not necessarily cancerous, for example, cystic of the pancreas, splenic tumor or enlargement of the spleen, etc... (Stedman's medical dictionary, 25th ed, 1990, p.1652-1653), the encompassed claimed method uses metastatic cells from any abnormal growth of prostate.

The nature of the invention

The nature of the invention is complex. Although the specification discloses SEQ ID NOs: 3, 4, 6, 8, 10, the claims however encompass any variants of the alpha-methylacyl-CoA racemase mRNA with unknown structure and function, having unknown expression level in prostate cancer. Further, the probes for use in the claimed method encompasses unknown sequences attached to a fragment complementary to SEQ ID NO:3.

The state of the prior art

Although the prior art (US 6,395,278, of record) teaches SEQ ID NO:107 of 1621 nucleotide in length, which is 99.9% similar to SEQ ID NO:3, and which overexpresses in prostate cancer, and screening for candidate antisense that decreases the expression of SEQ ID NO:107, the art does not teach that SEQ ID NO:107 is overexpressed in metastatic prostate cancer cells, nor contemplates or suggests screening for candidate antisense using a sample comprising metastatic prostate cancer cells, especially in view that the level of expression of a polynucleotide in a metastatic cancer cells cannot be predicted, when based solely on its expression level in corresponding primary cancer cells (see Zhau, HE, 1994, J Cell Biochem, Suppl 19: 208-216; Russo, V et al, 1995, Int J Cancer, 64: 216-221).

The level of one of skill in the art

Although the level of skill in the field of molecular pathology is high, it would be undue experimentation for one of skill in the art to practice the claimed invention.

The level of predictability of the art

The level of unpredictability is high.

One cannot predict that the alpha-methylacyl-CoA racemase mRNA variants would be correlated with prostate cancer, because one cannot predict that the claimed variants would overexpress in prostate cancer. It is well known in the art that variants of a sequence do not necessarily express at the same level as the corresponding wild type. For example, Schmid S et al, 2001 (J comparative Neurology, 430(2): 160-71), teach that the variants flip/flop of the gene GluR are expressed at higher levels in neurons in the auditory braistem, as compared to the wild type GluR-A and GluR-B, and that neurons in the central nucleus of the inferior collicullus express high levels of GluR-B flip but only low levels of the other receptor subunits. Conner et al, 1996 (Mol Brain Res, 42: 1-17), teach that full length trkB is found the hippocampus in patients with Alzheimer's disease, but not in hippocampi of either normal age-matched individual or patients with Huntington's disease, and that truncated trkB is found in senile plaques in hippocampus and temporal lobe in both patients with Alzheimer's disease and Huntington's disease, but not in normal brains of aged-matched individuals (page 8, item 3.1.2). Thus in view of the teaching in the art one cannot predict that the alpha-methylacyl-CoA racemase mRNA variants would be overexpressed in prostate cancer and correlated with prostate cancer. Since one cannot predict that the alpha-methylacyl-CoA racemase mRNA variants would

be correlated with prostate cancer, one cannot predict that the screened inhibitors of said variants would be useful for treating prostate cancer.

Further, one cannot predict that the claimed probe comprising a small fragment of SEQ ID NO:3 of 15, 20, 25, 30, 40, 50 or 75 in length would be specific for SEQ ID NO:3, in view that the claimed probe encompasses unknown sequences attached only to a small fragment of SEQ ID NO:3, which probe would readily hybridize under the stringent conditions cited in claim 34 with unknown sequences comprising said probe.

In addition, one cannot predict that prostate tumor cells would be metastatic, in view that tumor cells encompass cells with only abnormal growth, supra.

Working example, and the amount of direction provided by the inventor

The specification discloses the structure of the alpha-methylacyl-CoA racemase mRNA SEQ ID NO: 3 and variants thereof of SEQ ID Nos: 4, 6, 8, 10. The specification discloses that SEQ ID NO:3 is overexpressed in primary and metastatic prostate.

The specification, however, does not disclose how to make and use the claimed numerous nucleic acid variants which are capable of functioning as that which is being disclosed, in view a lack of a disclosure of which region of SEQ ID NO:3 confers the racemase function of SEQ ID NO:3. The specification does not disclose that the alpha-methylacyl-CoA racemase mRNA variants are overexpressed in prostate cancer. Further, Applicant has not taught what the structure is for the sequences attached to a complementary fragment SEQ ID NO:3.

It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as

well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the above unpredictability, the lack of adequate disclosure in the specification, and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
June 15, 2006

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER